Remarks

Applicants acknowledge with appreciation the decision by the Patent Office to reset the period for response to the Office Action mailed July 30, 2002 (Paper No. 22) because the revocation of power of attorney was not processed by the Patent Office, resulting in the Office Action being sent to Applicants' previous representative. In light of the delay in obtaining the Office Action, the time for response was reset by the Patent Office and the present Office Action was mailed on October 18, 2002.

Applicants acknowledge the indication made in the Office Action dated October 18, 2002 that the request for continued examination has been entered. The claims have been amended to recite "oligonucleotide" instead of "nucleic acid" to more particularly point out the claimed invention. Support for oligonucleotide may be found throughout the specification and, for example on page 5, lines 26-29. Upon entry of the foregoing amendment, claims 1, 3, 4, 6-16 and 18-21 will be pending.

Response to Declaration

Applicants acknowledge, with appreciation, withdrawal of the previous rejection under 35 U.S.C. 103 based on Hatzenbuhler (U.S. Patent 5,275,946) and Padmapriya (U.S. Patent 5,929,226) in view of the Declaration dated August 23, 2001 by Steven Gatton.

Rejection of Claims under 35 U.S.C. 103(a)

Claims 1, 3-4 and 6-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan (U.S. Patent 5,747,663) in combination with Su (U.S. Patent 5,804,684). Applicants respectfully request reconsideration and withdrawal of the rejection insofar as it may be applied to the amended claims.

The pending claims have been amended to recite a method for desalting and concentrating an oligonucleotide comprising various steps [emphasis added]. Applicants respectfully submit that nothing in any of the cited references, either alone or in combination, teaches or suggests the claimed methods for desalting and concentrating an oligonucleotide.

The Colpan reference is directed to processes for the removal of endotoxins from preparations of DNA or RNA isolated from host cells. As stated in the Office Action, "Colpan further teaches that samples that are suitable for purification include nucleic acids such as RNA, YACs and genomic DNA obtained from cells, cell organelles, tissues or microorganisms" (see Office Action at page 4, first paragraph). Applicants respectfully assert that the claims, as amended, distinguish the invention over Colpan because the limitations present in the claims as currently amended are neither taught nor

suggested in Colpan. Oligonucleotides are defined in the specification, as nucleic acid molecules "comprising from about 1 to about 100 nucleotides, more preferably from 1 to 80 nucleotides, and even more preferably from about 4 to about 35 nucleotides" (see page 5, lines 26-28).

Nothing in Colpan suggests the claimed method for desalting and concentrating an oligonucleotide because oligonucleotides are simply not taught in this reference. A person having ordinary skill in the art would not have been motivated to modify Colpan for the purpose of developing a method for desalting and concentrating an oligonucleotide because Colpan is directed to the purification of nucleic acids such as RNA, YACs and genomic DNA obtained from cells, cell organelles, tissues or microorganisms. The methods taught in Colpan are entirely different from the claimed methods because their objective is different and the chemical entity that is being purified in Colpan is different.

The Su reference is relied on for its purported disclosure of modified hydrophobic polymers such as polyethylene, polyvinyl and polypropylene in the purification of nucleic acids from biological sources (see Office Action at page 4, third paragraph). Applicants respectfully assert that the Su reference does not teach or suggest the claimed method for desalting and concentrating an oligonucleotide, either alone or in combination with Colpan because there would have been no motivation to combine what is taught in Su with the disclosure in Colpan.

Furthermore, nothing in the Su reference or the Colpan reference teaches or suggests rinsing the hydrophobic base matrix with an unbuffered aqueous solution as is required in step (c) of claim 1. Neither of the two cited references would have therefore motivated a person having skill in the art to combine these two references to arrive at the claimed invention because the limitations present in the claims are not taught or suggested in either of the two references. Even if such a motivation to combine the references did exist, the disclosure of the combined references does not teach or suggest all the limitations of the claims. For these reasons, Applicants respectfully request that the rejection be reconsidered and withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at his convenience.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "version with markings to show changes made" as required. If there are any additional fees due in connection with the filing of this response, please

charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
Morgan, Lewis & Bockius LLP

Dated: April 17, 2003
Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Ave. NW
Washington, D.C. 20004

Robert Smyth
Registration No. 50,801

Version With Markings To Show Changes Made

1. (Amended) A method of desalting and concentrating an oligonucleotide [~~nucleic acid~~] within a sample, said method comprising [~~the steps of~~]:

(a) subjecting the sample comprising [~~comprised of~~] the oligonucleotide [~~nucleic acid~~] to anion exchange purification to obtain a purified sample;

(b) contacting the purified sample with a binding medium comprising a strongly hydrophobic base matrix selected from the group consisting of polydivinylbenzene, poly(styrene-divinylbenzene), polystyrene copolymers, polyethylene and polypropylene;

(c) rinsing the binding medium with an unbuffered aqueous solution; and

(d) eluting the oligonucleotide [~~nucleic acid~~] with an aqueous organic solvent.

2. (Cancelled)

3. (No Change) The method of claim 1, wherein the binding medium is a column comprised of particles having a diameter of about 1 micron to about 250 microns.

4. (No Change) The method of claim 3, wherein the binding medium is a column comprised of particles having a diameter of about 50 micron to about 75 microns.

5. (Cancelled)

6. (No Change) The method of claim 1, wherein the unbuffered aqueous medium is water.

7. (No Change) The method of claim 1, wherein the column is rinsed repeatedly to achieve an effluent conductivity following rinsing at or below 100 microSiemens/cm.

8. (No Change) The method of claim 1, wherein the column is rinsed repeatedly to achieve an effluent conductivity following rinsing at or below 25 microSiemens/cm.

9. (Amended) The method of claim 1, wherein the oligonucleotide [~~nucleic acid~~] has been modified with a compound selected from the group consisting of biotin, fluorescein and related dyes, spacers, thiol modifiers, carboxylate modifiers or any combination of these.

10. (Amended) The method of claim 1, wherein the oligonucleotide [~~nucleic acid~~] is selected from the group consisting of a DNA phosphodiester, phosphorthioate, methylphosphonate, 2'-O-methyl RNA, 2'-O-alkyl RNA, 2'-O-methyl DNA, 2'-O-alkyl DNA and chimeras containing such structures.

11. (Amended) The method of claim 1, wherein the oligonucleotide [~~nucleic acid~~] comprises nucleotide bases selected from the group consisting of 5'-methylcytidine, inosine, halogenated uridines, etheno-bases, dideoxynucleosides and inverted bases.

12. (Amended) The method of claim 1, wherein the oligonucleotide comprises [~~nucleic acid is comprised of~~] inverted 3'-5' linkages.

13. (Amended) The method of claim 1, wherein the oligonucleotide comprises [~~nucleic acid is comprised of~~] 5'-2' linkages.

14. (Amended) The method of claim 1, wherein the [~~nucleic acid is an~~] oligonucleotide comprises [~~comprised of~~] about 2 to 100 nucleotides.

15. (No Change) The method of claim 1, wherein the sample is the product of a strong ion exchange chromatography.

16. (No Change) The method of claim 1, wherein the sample is the product of a weak ion exchange chromatography.

17. (Cancelled)

18. (No Change) The method of claim 1, wherein the aqueous organic solvent is an alcohol selected from the group consisting of n-propanol, isopropanol and methanol.

19. (No Change) The method of claim 1, wherein the aqueous organic solvent is aqueous ethanol.

20. (Amended) A method of exchanging a cation associated with an oligonucleotide [~~a nucleic acid~~] in a sample comprising [~~the steps of~~]:

(a) contacting the oligonucleotide [~~nucleic acid~~] associated with a first cation with a binding medium comprising a strongly hydrophobic base matrix selected from the group consisting of polydivinylbenzene, poly(styrene-divinylbenzene), polystyrene copolymers, polyethylene and polypropylene;

(b) rinsing the oligonucleotide [~~nucleic acid~~] bound to the binding medium with an unbuffered aqueous solution prior to elution;

(c) contacting the bound oligonucleotide [~~nucleic acid~~] with a solution comprising [~~comprised of~~] a second cation; and

(d) eluting the oligonucleotide [~~nucleic acid~~] associated with the second cation from the binding medium, wherein the second cation effectively displaces the first cation in the eluted [~~effluent~~] sample.

21. (Amended) The method of claim 1, wherein the oligonucleotide [~~nucleic acid~~] is a monomer.